REMARKS/ARGUMENTS

The foregoing amendments in the specification and claims are of a formal nature, and do not add new matter.

Prior to the present amendment, Claims 28-40 were pending in this application and were rejected on various grounds. Claims 36 and 37 have been canceled without prejudice. The rejection of the remaining claims is respectfully traversed.

Applicants expressly reserve the right to pursue any canceled matter in subsequent continuation, divisional or continuation-in-part applications.

Specification

The specification has been amended to remove embedded hyperlink and/or other form of browser-executable code.

Priority

The Examiner had stated that Applicants were entitled to the priority of U.S. Application No. 09/946,374, filed September 4, 2001 based on chondrocyte re-differentiation assay (Example 150, Assay 110). Applicants respectfully submit that the chondrocyte re-differentiation assay for support of patentable utility was first disclosed in International Application No. PCT/US00/04342, filed on February 18, 2000, the priority of which is claimed in the present application. Accordingly, the present application is entitled to at least the February 18, 2000 priority. In support, page 523 of the PCT publication, WO 00/78961, corresponding to PCT Application No. PCT/US00/04342, is enclosed herewith.

Claim Rejections – 35 U.S.C. §112, First Paragraph

Claims 28-32 and 39-40 are rejected under 35 U.S.C. §112, first paragraph, because "while being enabling for an isolated polypeptide comprising the polypeptide sequence set forth in SEQ ID NO:116, does not reasonably provide enablement for an isolated polypeptide having at least 80%, 85%, 90% or 95% identity to the polypeptide of SEQ ID NO:116." (See page 3 of the instant Office Action). The Examiner further alleges that "[t]he specification does not enable

any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope." Applicants respectfully disagree.

Without acquiescing to the Examiner's position, and solely in the interest of expediting prosecution in this case, Claims 28-32 (and, as a consequence, those claims dependent from the same) have been amended to recite a polypeptide that "induce chondrocyte re-differentiation". Since the claimed genus is now characterized by a combination of structural and functional features, any person of skill would know how to make and use the invention without undue experimentation based on the general knowledge in the art at the time the invention was made. As the M.P.E.P. states, "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation" *In re Certain Limited-charge cell Culture Microcarriers, 221 USPQ 1165, 1174* (Int'l Trade Comm'n 1983), *aff'. sub nom., Massachusetts Institute of Technology v A.B. Fortia,* 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985) M.P.E.P. 2164.01. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claim Rejections – 35 U.S.C. §112, First Paragraph

Claims 28-33, 36 and 39-40 are rejected under 35 U.S.C. §112, first paragraph, for alleged lack of sufficient written description. The Examiner asserts that "Claims 28-32 are drawn to an isolated polypeptide that shares '80%, 85%, 90%, 95% or 99%' identity to the polypeptide of SEQ ID NO:116, and Claims 33, 36 and 37 are drawn to an isolated polypeptide comprising the extracellular domain of the polypeptide of SEQ ID NO:116. However, the instant specification only describes the structure of the polypeptide of SEQ ID NO:116, and therefore, conception is not achieved until reduction to practice has occurred" (see page 4 of the instant Office Action).

Applicants submit that the cancellation of Claims 36 and 37 renders the rejection of these claims moot.

Without acquiescing to the Examiner's position, and solely in the interest of expediting prosecution in this case, Claims 28-32 (and, as a consequence, those claims dependent from the

same) are amended to recite a polypeptide that "induces chondrocyte re-differentiation". Furthermore, as amended, Claims 28-33 (and, as a consequence, those claims dependent from the same) no longer recite the term "extracellular domain". Therefore, the recited biological activity, coupled with a well defined, and relatively high degree of sequence identity is believed to sufficiently define the claimed genus, such that one skilled in the art would readily recognize that the Applicants were in the possession of the invention claimed at the effective filing date of this application. The Examiner is therefore respectfully requested to reconsider and withdraw the present rejection.

Claim Rejections – 35 U.S.C. §102

Claims 28-40 are rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Baker *et al.*, WO 00/12708 (publication date March 9, 2000).

Applicants submit that cancellation of Claims 36 and 37 renders the rejection of these claims moot. Furthermore, Claims 28-32 (and, as a consequence, those claims dependent from the same) have been amended to recite a functional limitation that the polypeptide "induces chondrocyte re-differentiation."

As discussed above, Applicants are entitled to an effective filing date of February 18, 2000. Accordingly, Baker *et al.* is not prior art under 102(b) since its publication date is after the effective priority date of the present application. Hence, Applicants respectfully request that this rejection be withdrawn.

Claims 28-34, 39-40 are rejected under 35 U.S.C. §102(a) as being allegedly anticipated by Yang *et al.*, WO 01/51638 (publication date July 19, 2001). As discussed above, Applicants are entitled to an effective filing date of February 18, 2000. Accordingly, Yang *et al.* is not prior art under 102(a) since its publication date is after the effective priority date of the present application. Hence, Applicants respectfully request that this rejection be withdrawn.

All claims pending in the present application are believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (Attorney's Docket No. **39780-2830 P1C5**). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: September 20, 2004

By: _____
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EXAMPLE 149: Detection of PRO Polypeptides That Affect Glucose or FFA Uptake by Primary Rat Adipocytes (Assay 94)

This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by adipocyte cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by adipocytes would be beneficial including, for example, obesity, diabetes or hyper- or hypo-insulinemia.

In a 96 well format, PRO polypeptides to be assayed are added to primary rat adipocytes, and allowed to incubate overnight. Samples are taken at 4 and 16 hours and assayed for glycerol, glucose and FFA uptake. After the 16 hour incubation, insulin is added to the media and allowed to incubate for 4 hours. At this time, a sample is taken and glycerol, glucose and FFA uptake is measured. Media containing insulin without the PRO polypeptide is used as a positive reference control. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as stimulators of glucose and/or FFA uptake in this assay: PRO1265, PRO1283, PRO1279, PRO1303, PRO1306, PRO1325, PRO1565 and PRO1567.

The following PRO polypeptides tested positive as inhibitors of glucose and/or FFA uptake in this assay: PRO1194, PRO1190, PRO1326, PRO1343, PRO1480, PRO1474, PRO1575 and PRO1760.

EXAMPLE 150: Chondrocyte Re-differentiation Assay (Assay 110)

This assay shows that certain polypeptides of the invention act to induce redifferentiation of chondrocytes, therefore, are expected to be useful for the treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis. The assay is performed as follows. Porcine chondrocytes are isolated by overnight collagenase digestion of articulary cartilage of metacarpophalangeal joints of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm^2 in Ham F-12 containing 10% FBS and 4 μg/ml gentamycin. The culture media is changed every third day and the cells are then seeded in 96 well plates at 5,000 cells/well in 100μl of the same media without serum and 100 μl of the test PRO polypeptide, 5 nM staurosporin (positive control) or medium alone (negative control) is added to give a final volume of 200 μl/well. After 5 days of incubation at 37°C, a picture of each well is taken and the differentiation state of the chondrocytes is determined. A positive result in the assay occurs when the redifferentiation of the chondrocytes is determined to be more similar to the positive control than the negative control.

The following polypeptide tested positive in this assay: PRO1265, PRO1250, PRO1430, PRO1356, PRO1275, PRO1274, PRO1286, PRO1273, PRO1283, PRO1279, PRO1306, PRO1325, PRO1343, PRO1418, PRO1565, PRO1474, PRO1787, PRO1556 and PRO1801.

EXAMPLE 151: Induction of Pancreatic β-Cell Precursor Proliferation (Assay 117)

This assay shows that certain polypeptides of the invention act to induce an increase in the number of pancreatic β-cell precursor cells and, therefore, are useful for treating various insulin deficient states in mammals, including diabetes mellitus. The assay is performed as follows. The assay uses a primary culture of mouse fetal pancreatic cells and the primary readout is an alteration in the expression of markers that represent